UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,870	03/07/2001	Mary H. Romans	NERV-00100	5447

7590 08/11/2004

J. Wendy Davis, Ph.D
Bracewell & Patterson, LLP
P.O. Box 61389
Houston, TX 77208-1389

EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,870	ROMANS, MARY H.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06/07/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-27* is/are pending in the application.

4a) Of the above claim(s) *10-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *none* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 06/07/04 has been entered. Claims 1-9 have been cancelled. Claims 18-27 have been added. Claims 10-17 are withdrawn as being drawn to a non-elected invention. Claims 10-27 are pending and claims 18-27 are under current consideration.

Claim Objections

The objection to claim 8 set forth on page 4 of the previous office action is withdrawn.

Claim Rejections - 35 USC § 101

The rejection of claim 5 under 35 USC 101 as being drawn to non-statutory subject matter is withdrawn. Claims are no longer drawn to humans.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to provide literal support for the term "non-transgenic" or "non-transenically". While the methodology taught in the

specification teaches the use on non-transgenic animals, the specification does not support the exclusion of transgenesis.

The rejection of claims 1-9 under 35 U.S.C. 112, first paragraph as it applies to newly added claims 18-27 is maintained, because the specification, while being enabling for a method of making a non-human mammal comprising non-traumatically and non-surgically compressing the tibial nerve such that allodynia is achieved or compressing the saphenous nerve via a surgical procedure such that hyperalgesia is achieved, does not reasonably provide enablement for any other model encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The newly added claims have limited the scope of the claims to non-human mammals. Applicant's arguments have been fully considered and are not persuasive for all other aspects of the scope of enablement rejection set forth on pages 5-9 of the previous office action mailed 03/10/2004.

Applicant has argued that it is within the skill of the ordinary artisan to inject a gel substance other than collagen around a nerve (page 7, 2nd paragraph) and claims are limited as such.

In response, the claims are not limited to a gel substance. For example, claims 18 and 23 do not recite at all that a substance be injected around the nerve. Furthermore, as set forth on pages 6-7 of the previous office action (refer specifically to page 7, 1st paragraph), the claims encompass injection of substances other than a gel that can

indirectly cause compression on a nerve. The claims are not limited to a gel, as Applicant has argued. While the specification has taught injection of a gel, claims are not limited to what is disclosed to the specification and thus, the specification fails to enable the full scope of the claims.

Applicant has argued that the compression of any nerve will result in pain. Applicant has argued that it is known by the skilled artisan that the peripheral nerves in a mammalian species are physiologically and anatomically similar and that the methods taught for the tibial and saphenous nerves are enabling for any peripheral nerve (page 7, paragraph 4). Applicant argues that Lundborg is inappropriately cited (refer to page 9 of the previous office action mailed 03/10/2004) in teaching that compression of the median nerve fails to result in pain (page 7, paragraph 3). Applicant believes that the compression applied by Lundborg is traumatic and differs from the instant invention.

In response, the specification has demonstrated that compression of different nerves results in different effects. For example, compression of the saphenous nerve results in hyperalgesia while compression of the tibial nerve results in allodynia. Furthermore, with respect to Applicant's disqualification of Lundborg, Applicant has failed to distinguish the compression applied by Lundborg from the compression of the instant claims. Applicant appears to give a subjective opinion that the compression of Lundborg is traumatic, despite no apparent trauma to the subject. It would appear that the methods of Lundborg consisting of applying external pressure without invasion of the body is less traumatic than the claimed methods comprising incision and injection of a substance around a nerve. The specification defines non-traumatic as nondestructive (refer to page 2, last paragraph). The compression of Lundborg is not destructive to the

medial nerve. The claims fail to distinguish the compression of the instant invention from that of the art. It is not apparent how the compression of the medial nerve by Lundborg is different from the compression of the saphenous and tibial nerves of the instant invention. Without some demonstration that the nerve compression of Lundborg is somehow different from the compression of the instant claims such that the lack of pain resulting from Lundborg's compression is inapplicable to the instant invention, the claims are not enabled for the full scope of the claims including any nerve other than the tibial and saphenous nerves.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Newly added claims 18-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The previous rejection of cancelled claim 5 is maintained as it applies to claims 18-27. It is not clear if the term "non-traumatic" is applicable to the animal or to the nerve. For example, incision into the leg is trauma to the animal but not necessarily to the tibial nerve.

Claims 18-27 are unclear because it is not known what is meant by the phrase "physiologic change" in claims 18 and 23. A physiologic change is generally accepted as a physiological alteration like swelling, cellular composition or other alteration in the body itself. Claims 22 and 27 limit the physiologic change to allodynia and hyperalgesia,

which are responses or effects of a physiologic change but are not generally considered physiologic changes themselves. Thus, the phrase "physiologic change" is unclear.

Claims 23-27 are unclear because the metes and bounds of what is encompassed by the phrase "around the nerve" are unclear. It is not known what distance around the nerve is encompassed by the claims.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's arguments and amendments to the claims, the previous rejections under 35 USC 102(a) and 102(b) are withdrawn. However, the new claims include specific embodiments that did not have to be considered in the previous office action. Therefore, a new rejection is set forth below.

Claims 18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Reyna (1999, ICLAS, Palma de Malloren, May 26-28, page 226).

Claim 18 is drawn to a method for producing a non-human mammalian model for persistent pain by altering a nerve non-traumatically such that a physiologic change associated with persistent neurogenic pain is produced. Claim 23 is directed to the non-human mammalian model.

Reyna taught introducing a proprietary biocompatible, non-irritating substance near the tibial nerve, which constitutes a non-traumatic nerve alteration. The plantar hind

paws were then tested for allodynia, a physiologic change associated with persistent neurogenic pain (paragraph 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyna (1999, ICLAS, Palma de Malloren, May 26-28) in view of Ford (1986, Laryngoscope, Vol. 96, pages 1248-1257).

Claims are drawn to a method for producing a non-human mammalian model for persistent pain by altering a nerve non-traumatically such that a physiologic change associated with persistent neurogenic pain is produced. Claim 19 limits the altering to injection of a gel. Claim 20 limits the gel to collagen. Claim 21 limits the nerves altered to the tibial, saphenous or other peripheral nerve of the lower extremity. Claim 22 limits the physiologic change to allodynia and hyperalgesia. Claims 23-27 is directed to the non-human mammalian model made by claims 18-22.

Reyna taught introducing a proprietary biocompatible, non-irritating substance near the tibial nerve, which constitutes a non-traumatic nerve alteration. The plantar hind paws were then tested for allodynia, a physiologic change associated with persistent neurogenic pain (paragraph 2). Reyna did not teach that the proprietary biocompatible substance was a gel or a collagen gel.

However, Ford taught injection of bovine collagen into the vocal cords to correct glottic insufficiency. Ford taught that collagen is safe, effective, easily injected and well tolerated (Abstract, page 1248, col. 2, paragraph 2) and that it attracts the ingrowth of fibroblasts allowing for deposition of new collagen (Abstract).

Accordingly, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to make the claimed mammalian pain model as taught by Reyna wherein the proprietary substance taught by Reyna is replaced with the collagen taught by Ford. One of ordinary skill in the art would have been sufficiently motivated to replace the proprietary substance with collagen due to its properties of inducing minimal immune response from the host animal, easy use and its ability to recruit fibroblasts that secrete new host collagen around the nerve where it is placed.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

AU1632